Amendments to the Specification

Please amend the specification as follows:

On page 1, please replace the paragraph at lines 9-29 with the following replacement paragraph:

A variety of immune factors ~~influences~~ influence the susceptibility of CD4 T cells to HIV-1 infection, including soluble factors and the state of T cell differentiation. Evidence for the importance of these host factors includes the observation that lymphocytes from different donors are not equally infectable with HIV-1, raising the possibility that resistance of lymphocytes to HIV I infection in vitro might be associated with different rates of disease progression (Spira, A. I. and D. D. Ho. 1995. *J. Virol.* 69:422; and Wainberg, M. A., N. Blain, and L. Fitz-Gibbon.1987. *Clin. Exp. Immunol.* 70:136). Host factors that are recognized to affect the susceptibility of CD4 cells to HIV infection include factors intrinsic to the CD4 cell and indirect factors. Among the direct factors of recognized importance are CD4 and fusion coreceptors(s) expression. The density of CD4 receptors expressed on the cell surface influences the efficiency of HIV-1 infection (Kabat, D., 1994. J. Virol. 68:2570; and Brand, D., 1995. *J. Virol.* 69:166). Recently chemokine receptors have been identified as a critical determinant of susceptibility to infection with HIV-1. Macrophage-tropic strains of HIV-1 utilize CCR5 as a fusion cofactor (Alkhatib, G., 1996, *Science* 272:1955; Doranz, B. J., 1996 *Cell* 85:1149; Choe, H., 1996. *Cell* 85:1135; Dragic, T., 1996. *Nature* 381: Deng, H., 1996. *Nature* 381:661) while T cell tropic strains of HIV-1 employ CXCR4/fusin as a coreceptor (Feng, Y., 1996. *Science* 272:872). The importance of these coreceptors is illustrated by the recent

observation that some multiply exposed individuals who remain uninfected with HIV-1 have mutations in CCR5 (Liu, R., 1996. *Cell* 86:367; Dean, M., 1996. *Science* 273:1856).

On page 9, please replace the paragraph at lines 14-35 with the following replacement paragraph:

Fusion proteins within the scope of the invention can be prepared by expression of a nucleic acid encoding the fusion protein in a variety of different systems. Typically, the nucleic acid encoding a B7 fusion protein comprises a first nucleotide sequence encoding a first peptide consisting of a B7 molecule or a fragment thereof and a second nucleotide sequence encoding a second peptide corresponding to a moiety that alters the solubility, binding, stability, or valency of the first peptide, such as an immunoglobulin constant region. Nucleic acid encoding a peptide comprising an immunoglobulin constant region can be obtained from human immunoglobulin mRNA present in B lymphocytes. It is also possible to obtain nucleic acid encoding an immunoglobulin constant region from B cell genomic DNA. For example, DNA encoding Cγ1 or ~~Cg4~~ Cγ4 can be cloned from either a cDNA or a genomic library or by polymerase chain reaction (PCR) amplification in accordance standard protocols. A preferred nucleic acid encoding an immunoglobulin constant region comprises all or a portion of the following: the DNA encoding human Cγ1 (Takahashi, N.S. et al. (1982) *Cell* 29:671-679), the DNA encoding human Cγ2; the DNA encoding human Cγ3 (Huck, S., et al. (1986) *Nucl. Acid Res.* 14:1779); and the DNA encoding human Cγ4. When an immunoglobulin constant region is used in the B7 fusion protein, the constant region can be modified to reduce at least one constant region mediated biological effector function. For example, DNA encoding a Cγ1 or Cγ4 constant region can be modified by PCR mutagenesis or site directed mutagenesis. Protocols and reagents for site

directed mutagenesis systems can be obtained commercially from Amersham International PLC, Amersham, UK.

On page 12, please replace the paragraph at lines 32-37 with the following replacement paragraph:

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques such as calcium phosphate or calcium ~~choloride~~ chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming host cells can be found in Sambrook et al. (*Molecular Cloning: A Laboratory Manual*, 2nd Edition, Cold Spring Harbor Laboratory press (1989)), and other laboratory textbooks.

On page 13, please replace the paragraph at lines 14-20 with the following replacement paragraph:

B7 molecules or B7 Ig fusion proteins produced by recombinant technique may be secreted and isolated from a mixture of cells and medium containing the protein. Alternatively, the protein may be retained cytoplasmically and the cells harvested, lysed and the protein isolated. A cell culture typically includes host cells, media and other byproducts. Suitable ~~mediums~~ media for cell culture are well known in the art. Protein can be isolated from cell culture medium, host cells, or both using techniques known in the art for purifying proteins.

On page 13, please replace the paragraph at lines 29-37 continuing onto page 14, lines 1-11 with the following replacement paragraph:

In another embodiment of the invention, a natural ligand of CD28 (B7-1, B7-2) can be presented to T cells in a form attached to a solid phase surface, such as beads. The B7

molecules, fragments thereof or modified forms thereof capable of binding to CD28 and costimulating the T cells (e.g., B7 fusion proteins) can be prepared as described for the soluble B7 forms. These molecules can then be attached to the solid phase surface via several methods. For example the B7 molecules can be crosslinked to the beads via covalent modification using tosyl linkage. In this method, B7 molecules or B7 fusion proteins are in ~~0.,05M~~ 0.05M borate buffer, pH 9.5 and added to tosyl activated magnetic immunobeads (Dynal Inc., Great Neck, NY) according to manufacturer's instructions. After a 24 hr incubation at 22°C, the beads are collected and washed extensively. It is not mandatory that ~~immunmagnetic~~ immunomagnetic beads be used, as other methods are also satisfactory. For example, the B7 molecules may also be immobilized on polystyrene beads or culture vessel surfaces. Covalent binding of the B7 molecules or B7Ig fusion proteins to the solid phase surface is preferable to adsorption or capture by a secondary monoclonal antibody. B7Ig fusion proteins can be attached to the solid phase surface through anti-human IgG molecules bound to the solid phase surface. In particular, beads to which anti-human IgG molecules are bound can be obtained from Advanced Magnetics, Inc. These beads can then be incubated with the B7Ig fusion proteins in an appropriate buffer such as PBS for about an hour at 5°C, and the uncoupled B7Ig proteins removed by washing the beads in a buffer, such as PBS.

On page 18, please replace the paragraph at lines 8-20 with the following replacement paragraph:

~~Polycolonal~~ Polyclonal antibodies to a purified protein or peptide fragment thereof can generally be raised in animals by multiple subcutaneous (sc) or intraperitoneal (ip) injections of an appropriate immunogen, such as the extracellular domain of the protein, and an adjuvant. A polyclonal antisera can be produced, for

example, as described in Lindsten, T. et al. (1993) *J. Immunol.* 151:3489-3499. In an illustrative embodiment, animals are typically immunized against the immunogenic protein, peptide or derivative by combining about ~~1 mg to 1mg~~ 1 μg to 1 g of protein with Freund's complete adjuvant and injecting the solution intradermally at multiple sites. One month later the animals are boosted with 1/5 to 1/10 the original amount of immunogen in Freund's complete adjuvant (or other suitable adjuvant) by subcutaneous injection at multiple sites. Seven to 14 days later, the animals are bled and the serum is assayed for anti-protein or peptide titer (e.g., by ELISA). Animals are boosted until the titer plateaus. Also, aggregating agents such as alum can be used to enhance the immune response.

On page 34, please replace the paragraph at lines 35-37 and continuing onto page 35, lines 1-13 with the following replacement paragraph:

Purified CD4+ lymphocytes were obtained from uninfected donors as described in, for example, C. H. June et al. (1987) *Mol. Cell. Biol.* 7:4474, and B. L. Levine et al. (1995) *Int. Immunol.* 7:891 (1995). The purified cells were stimulated with ~~DYNAL M-450~~ DYNAL ® M-450 beads coated via tosyl conjugation with equal quantities of αCD3 (OKT3, mouse IgG2a, American Type Tissue Collection), and αCD28 (9.3, mouse IgG2a) (4). Alternatively, purified CD4+ cells were stimulated with phytohemagglutinin [PHA, 5 μ g/ml (Sigma)] and 100 units/ml IL-2 (Boehringer Mannheim). Three days after stimulation, 7 x 10^6 CD4 cells stimulated with αCD3/αCD28 (open symbols; Figure 1) or PHA/IL-2 (filled symbols; Figure 1) were infected with 1 x 10^4 $TCID_{50}$ (median tissue culture infectious dose) of HIV_{US1} (squares; Figure 1) or with 1 x 10^4 MAGI (described in, for example, J. Kimpton, et al. (1992) *J. Virol.* 66:2232) infectious doses of HIV_{NL4-3} (circles; Figure 1). After 2 hours at 37°C, the cells were washed three times and refed with 50% conditioned medium to a final concentration of 1 x 10^6 cells/ml. At the

designated time points, cleared supernatant was analyzed for the presence of $p24_{Gag}$ antigen by ELISA (Coulter). Each experiment was done at least 5 times, and representative values are depicted.